UNOFFICIAL TRANSCRIPT*
WASHINGTON STATE PHARMACY AND THERAPEUTICS COMMITTEE MEETING

February 16, 2005
Radisson Hotel SeaTac
9:00am – 2:30pm

Committee Attendance:
Daniel Lessler, M.D. (Chair)
Robert Bray, M.D.
T. Vyn Reese, M.D.
Angelo Ballasiotes, Pharm.D.
Alvin Goo, Pharm.D.
Jason Iltz, Pharm.D.
Janet Kelly, Pharm.D.
Patti Varley, ARNP
John White, Pharm.D. (Via teleconference)

Quorum was shown for all Pharmacy & Therapeutics Committee motions, 2nd's, and votes.

9:00 a.m. - Committee came to order.

Welcome and Introductions

- Daniel Lessler, M.D., welcomes the committee and announces that John White, Pharm.D would be joining the committee via telephone. Reminds that since there is now a full transcription of the proceedings of each session and there are no minutes which need approval, he does comment that transcription is outstanding and that he appreciates the work and is very well written.
- Jeff Graham, M.D., consultant to the Health Care Authority, announces that information from Consumer Reports has been distributed. The reports contains information about different drug classes, however, Dr. Graham asks that the committee members not read the reports before decisions are made, although they do refer to evidence based medicine, this is just for interest and information.
- The committee members introduce themselves.
- Dr. Lessler reminds those in the audience that there is a sign up sheet for stakeholder input, also that any people that do speak they must limit their comments to three minutes and finally as indicated in the agenda the committee will be returning to the discussion on antidepressants and making a decision. Dr. Lessler asks that if there are speakers who presented during the last meeting who have no new information that they refrain from speaking at this meeting in the interests of time and they should be aware that their comments form the last meeting were well captured in the transcripts of the last meeting. If there are stakeholders with new information to share then the committee welcomes the input.

AIIRA

Update of Drug Class Review

- Dr. Furmaga of OHSU joins by conference phone to deliver the presentation
- Dr. Lessler opens the discussion to committee members.
- T. Vyn Reese, M.D., asks Dr. Furmaga to confirm whether the drugs losartan, valsartan, and candesartan are the only three that have shown efficacy for congestive heart failure.
- Dr. Furmaga responds that while she does believe the other drugs can be excluded, those are the three with the data. The Elite Trials were constructed to prove that losartan was superior to captopril and that with that trial it would not be possible to prove them equivalent as the trials was not set up in that manner. She explains that valsartan and

* For copies of the official audio taped record of this meeting, please contact Erika Clayton at (206)521-2027 pdp@hca.wa.gov.

candisartan are beneficial in patients with heart failure but that the evidence for losartan in inconclusive in that regards.

- Dr. John White asks if the rates of angioedema are equivalent between the two groups.
- Dr. Furmaga explains that the mention of angiodema is very rare. The incidence of angiodema is much less in patients who are on an ace inhibitor and in some trials patients who had ace inhibitor induced angiodema, she says, you can have an angiodema with an ARB.
- Dr. White asks her to clarify whether or not the incidence of angiodema is lowered with the use of ARB's.
- Dr. Furmaga says that this is true and that the incidence is .1 percent.
- Robert Bray, M.D., comments that Dr. Furmaga concluded that there was no evidence for olmesartan for any question; however, he found that in summary table 9 of the report on page 44, there was no evidence for eprosartan on any of the questions.
- Dr. Furmaga responds that while there was some information for the safety of eprosartan in some adverse event trials, there were no trials that included over a thousand patients or were conducted for longer than a year for olmasartan that could be included in the adverse events. There was one article pulled on olmasartan which was actually a review of a number of different clinical trials looking at blood pressure reduction and safety information but it was not actually one clinical trial with more than a thousand patients.
- Dr. Bray thanks Dr. Furmaga for indicating the existence of safety data but asks for clarification regarding the absence of efficacy data for eprosartan for any of the indications that were reviewed.
- Dr. Furmaga confirms this absence.
- Alvin Goo, Pharm.D, asks for clarification regarding whether or not there is any benefit in using angiotensin receptor blockers as first line for any indication.
- Dr. Furmaga references a meta- analysis recently published which reviewed the trials of patients with heart failure and myocardial infarction which found there was no difference with the ace inhibitors and ARB's in all cause mortality or heart failure hospitalizations. The conclusion was that an ARB could be used interchangeably with an ace inhibitor and could be considered as first line. Dr. Furmaga also mentions a publication from the Heart Failure Society of America who considered the data of the meta-analysis and concluded though they could be considered interchangeable they would still use an ace inhibitor first line. Joint Commission has also come out with some indicators that accept an ace inhibitor or an ARB with patients who are post-MI or have heart failure, with the conclusion being that the patients can be put on an ace inhibitor or an ARB, they would accept either/or not one before the other. In regards to patients with diabetic nephropathy, there is little data for ace inhibitors and patients with type 2 diabetic nephropathy. There is data available on patients with type one diabetic nephropathy, the ADA has reported that an ARB can be used as first line in patients with type 2 diabetic nephropathy, however, there has also been a meta-analyses recently published looking at ace inhibitors versus ARB's and lumping together all the diabetic nephropathies and concluding that there is significant reduction in ARB's for renal outcome. However, the mortality outcomes are different than they would be with an ace inhibitor. It would then depend, when treating patients with diabetic nephropathy if the concern is placed on the cardiovascular and long-term outcomes or with renal outcomes.
- Dr. Goo asks for confirmation in regards to the idea of significant difference and whether that comes from the RENAAL results and the inclusion of secondary outcomes such as doubling as far as both the IDNT and the renal.
- Dr. Furmaga confirms this.
- Dr. Goo then asks if there is an idea of an absolute difference in the end stage renal disease.
- Dr. Furmaga comments that the relative risk for the ReNow end stage renal disease was a decrease of 28% versus placebo and for end stage renal disease and IDNT it was a decrease of 23% versus placebo.
- Dr. Goo asks if there is a way to calculate an absolute difference.
- Dr. Furmaga responds that she would have to get back to him on that calculation. She then wants to respond to the eprosartan question, in regards to the efficacy under patients with hypertension there were two trials of eprosartan that looked at quality of life so then it is not the long-term outcome.
- Dr. Bray comments that in that study it showed no improvement of quality of life.
- Dr. Furmaga confirms this comment.

Stakeholder Input

Dr. Lessler asks that the stakeholders keep comments to three minutes or less and that they identify any sponsors and submit all evidence to OHSU.

- Raed Fahmy, M.D., a cardiologist from Tacoma speaking on behalf of a pharmaceutical company for valsartan. In Tacoma, Dr. Fahmy belongs to a large group of cardiologists who have a large Medicaid patient population and he believes that valsartan is an easy drug to use in terms of side effects, which improves quality of care and compliance. He repeats that this drug has proven itself to be simple and easy to use and that he does not receive many complaints about this drug as a practicing cardiologist. In regards to data for hypertension, the Value Trial

has not been discussed but there is the data from Val-HeFT and the VALIANT Trials and all of this is important for those cardiologists who find this agent to be very useful for patients.

- Singh Lam, M.D., speaking on behalf of Novartis, commenting on losartan. He is a Medicaid provider practicing internal medicine in the International District and in North Seattle. Sixty percent of his patients are Medicaid patients and senior citizens, he believes that the decision that will be made at the meeting today will impact his patients and practice and finds losartan is comfortable to use. He explains that this drug has been on the market since 1996 and that he has been prescribing it since 1997, he knows what to expect in terms of its efficacy and safety. It has been proven effective in patients with congestive heart failure, prevention of renal disease in diabetic patients and also used in cardiovascular complications in patients with hypertension. The majority of Asian patients cannot tolerate Ace Inhibitors because of intractable cough. A cough occurs in very high proportion of Asian patients and bout 40% in his experience. He feels that an ARB is the only alternative in this group of patients. Not all ARB are singularly interchangeable, some are less effective, and some have not been proven to be effective in certain situations. Losartan appears to be indicated in patients with CHF in the recent trials. As a practitioner, he does not want to switch all his patients from Diovan or valsartan and he requests that the committee put it on the Preferred Drug List. He wants to be able to prescribe the ARB that he knows to be safe, effective and well tolerated and he is backed with extensive post marketing research.
- Michael Ring, M.D., a private practice cardiologist from Spokane, past president of the Spokane County Medical Society and currently director of the Cath Lab at Sacred Heart, has received an honorarium from Novartis to testify in favor of keeping valsartan- Diovan on the formulary. He comments that there are a several reasons why valsartan should remain on the formulary. He feels that the strength of the clinical trial data that Novartis has provided should be commended and that it is important to continue to sponsor these multiple trials. It is critical to demonstrate that not only has control over the use of medications been achieved, but, that it is now possible to prevent cardiovascular mortality in adverse events. He adds that since its post market approval Novartis has sponsored several large expensive multi-center randomized loss trials involving an approximate total of 50,000 patients and costing 800 million dollars. It is on the basis of these trials that we are actually hearing the data and considering continuing using these as an alternative to ace inhibitors for those who cannot tolerate them. Dr. Furmaga's data with Valheft showed that valsartan is certainly the equivalent to Captopril in regards to improving ejection fractions and decreasing New York Heart Association class congestive heart failure, improving the quality of life and reducing hospitalizations for congestive heart failure. More importantly, for the patients who cannot tolerate an ace inhibitor or were not on a valsartan, there was decreased overall mortality in heart failure morbidity by 44%, obviously very reassuring to those who care for heart failure patients. In the Valiant studies cited valsartan certainly proved to be the equal to the gold standard ace inhibitor captopril in decreasing mortality and cardiovascular morbidity and the current myocardial infarctions, hospitalizations for congestive heart failure. These are two high-risk groups, the congestive heart failure group and the post-MI patients with decreased LV function. The patients suffering from these indications are the ones who get into the most trouble and cardiologists would like to see a proven drug for these patients.
- Andy Weis, M.D., of Novartis Pharmaceuticals, regional council and associate director, has come to support the Novartis product, valsartan, the angiotensin receptor blocker with the trade name of Diovan. He first references the Value Trial, which Dr. Furmaga spoke about in her presentation, he mentions that this trial was published past the date of collection point and will probably be included in the next review done by OHSU. Value is a large trial in high-risk hypertension patients and in the report there was very little data in these types of patients. Value was a trial of over 15,000 patients over a period of three to four years randomized to receive either valsartan or amlodipine; it was the first trial of its kind to compare an ARB against the most widely used third generation dihydropyridine calcium channel blockers. The primary endpoint was a composite of significant cardiovascular events that could be found in a clinical situation. Although this study was initially powered for superiority in the end it showed equivalence to amlodipine in terms of the overall cardiovascular morbidity and mortality. Another significant finding of the study, while it was not a primary or secondary endpoint was a 23% wealth of risk reduction in an onset of new diabetes among those patients treated in the valsartan arm. While the way the study was constructed was certainly not to look at that aspect, it was proved to be true. The study was constructed using two titration arms, one for valsartan the other for amlodipine and was not a forced titration schedule. The dosing of valsartan that was used in the study was one based on the initial FDA approval before its enlaboring modifications hit within the last couple of years, it was also based on the dosing that was approved in the European Union at the time this study was conducted. Novartis started a new trial called Navigator, which uses the meglitinide compound, nateglinide under the trade name of Starlex. This study is being conducted to prove whether there is an affect of either valsartan or nateglinide when used separately or in combination to test a hypothesis of looking at the relative risk reduction in new onset diabetes. This trial is about 8,000 patients and only recently began, there is no data to share currently and the study will not be complete until 2008. He concludes by commenting that the Novartis product Diavan is the market leader with an over 40% market share within the U.S. and the largest market share within Washington State. He adds that he thinks if many patients were to be taken off valsartan it would create a

significant burden on the physicians and particularly on the pharmacists who would have to switch them to a new therapy.

- Donald Moran, M.D., a member of the Department of Medical Affairs at Sanofi Aventis Pharmaceutical, is speaking on behalf of himself and Sanofi Avenits Partners at Bristol Meyers Squibb who in tandem produce and manufacture the Angiotensin receptor blocker irbesartan, manufacture and distributed in this country under the names Avapro and Avalide. In deference to the wonderful presentation done by Dr. Furmaga, he has identified that his is one of seven products that adequately treats hypertension in this country. The reality is the treatment of hypertension in this country; represents a continuum of severity, the majority of outpatients require more than one agent for the control of their hypertension, in particular the most confounding condition being diabetes. Statistics and research have shown that the average diabetic patients requires 3.4 drugs to maintain and achieve their target blood pressure and retain it over a period of time. The significance of that is that irbesartan is unique in the sense that one of only two substances actually approved for a regulatory agent through the FDA as a real protective substance specific for diabetic nephropathy related to type 2 hypertension and diabetes mellitus. He also comments that he was pleased to hear Dr. Furmaga, when upgrading the quality of evidence, put the level of data behind irbesartan as good, the highest level of confidence. Secondly, to put in perspective the magnitude of the effect, to go back to Dr. Furmaga's point, on a relative basis compared to standard drug regimens, including the comparative drug amlodipine, the relative risk reduction in the halting of progression the amelioration of diabetic nephropathy was a 20% risk reduction. On a number needed to treat basis that is sixteen patients over a 2.6-year period. On the rubric of evidence based medicine that is an impressive pharmacologic endpoint, which cannot be denied. Also as Dr. Furmaga pointed out the questions of whether there are guidelines there for which Angiotensin receptor blockers might be first line treatments. He comments that he will not go down that path, however, he will acknowledge that through JNC7 and through the guidelines of the American Diabetic Association 2003 the angiotensin receptor blockers have achieved a new prominence in the treatment of hypertension associated with comorbid condition, diabetes being one, in particular type 2 diabetes, whereas a wealth of new evidence weighing and moving the pendulum in favor or Angiotensin receptor blockers. In the CDC surveillance data in the state of Washington, rated 21 out of 50 states, there have been added 1.5 new cases of patients with end stage renal disease due to diabetes alone to our roles everyday. That is a 23% increase in the rate in just four years. In conclusion he references Dr. Bruce Pasadie of University of Washington has weighed in on the subject of Therapeutic Equivalence and Class Effect on these drugs related to the renal Angiotensin system and published his findings in the journal circulation within the last year and half, he proceeds and recommends caution and explains to take strong data for morbidity or mortality in point for one or two drugs and extrapolate to a whole class is dangerous and recommends proceeding with caution. The FDA when given the opportunity to evaluate serving an end point, claims that renal end points involving urinary albumin excretion and other renal endpoints have been used as a basis for other manufacturers to promote their drug for diabetes have been censured for violations of the food and drug act. He recommends that the committee consider irbesartan as an important addition for the treatment of hypertension, one for which substitution is probably not indicated until more evidence is provided.
- Laurie McKenna, Health Science Consultant from Merck, testifying for Cozaar. She underscores some points regarding losartan. Cozar is indicated for the treatment of hypertension as are the rest of the ARB's under considerations, but Cozar is the only ARB indicated to reduce the risk of stroke in patients with hypertension and left ventricular hypertrophy, but there is evidence that this benefit does not apply to black patients. The evidence for this indication was based on the results of a live trial. Cozar is also indicated for the treatment of patients with type 2 diabetes and a history of hypertension, based upon the results of the ReNow Trials. Just as a review, the losartan intervention for end point reduction in hypertension or the live study was a multi-national double blind study comparing a regimen based on Cozar which was dosed once daily and a regimen based on atenolol in 9,193 hypertensive patients with UCG documented LVH. The primary endpoint was first occurrence of CB death non-fatal stroke or non-fatal MI, treatment of Cozar resulted in a 13% reduction in the risk of primary endpoint compared to the atenolol group, a 25% reduction in the risk of stroke relative to atenolol which again provided the evidence for the unique indication to reduce stroke in patients with hypertension and LVH. This 25% reduction in risk of stroke was an addition to the benefit in risk reduction in stroke that would have been seen with atenolol alone. There was no significant difference in the risk of MI receiving mortality between the two treatment groups and blood pressure reduction was similar in both groups. The ReNow Trial, or the reduction of endpoint is NIDDM, with the Angiotensin II receptor antagonists losartan was a randomized placebo control double blind multi-center study conducted in 1,513 patients with type 2 diabetes and nephropathy. Treatment with Cozar again dosed once daily, plus conventional antihypertensive therapy compared to treatment with placebo plus conventional therapy related in a 16% risk reduction in the primary endpoint of time to first occurrence in any one of the following events. Doubling of serum creatinine, ESRD, or death. There was a 25% reduction in the occurrence of sustained doubling of serum creatinine , a 29% reduction in end stage renal disease which was an absolute difference of 47 patients. There were 197 patients who developed end stage renal disease in the placebo group versus 147 in the losartan group. There was a 34% reduction in protein urea, an effect that was evident within three months of starting therapy. A 13% reduction in the rate of decline in the filtration rate also there was no significant

difference in the incidence of the composite endpoint of CB morbidity and mortality. Some cautions with this drug, when used in pregnancy during the second and third trimester drugs that act directly on the immuno-angiotensin system can cause injury and even death to the developing fetus and in the live trial adverse events with Cozar were similar to those reported previously for patients with hypertension, and for complete adverse experience information Ms. McKenna refers the committee to the accompanying package circular. In summary, she underscores the fact that losartan is indicated not only for the treatment of hypertension but is the only ARB indicated for the reduction of stroke in pts with hypertension and LVH and also indicated in type 2 diabetes.

- Derek Terada, Pharm.D., Medical Scientist speaking on behalf of Doehringer Ingelheim for telmisartan or Micardis. This is a competitive product, the pharmacokinetic profile of telmisartan, has the longest half life, is one of the more ibrofilic in class, the drug is less than 1% renally eliminated, and it is not necessary to make any dosage adjustment for patients with mild to moderate renal failure. In terms of efficacy, telmisartan has been shown to be effective in terms of blood pressure reduction compared to members of the class as well as other antihypertensive agents, in fact, Doehringer has one of the largest databases in terms of ambulatory blood pressure. Micardis that has shown efficacy in terms of trials with reducing ambulatory blood pressure during the daytime, nighttime, early morning hours and even the last couple hours of the dosing interval when given once a day. It is truly a once a day administered drug. The other important point not mentioned in the review, is the recently published trial in the New England Journal of Medicine which compared telmisartan to enalapril in terms of declining glamiliar filtration with five years diabetic nephropathy population and in that recent publication it was found that telmisartan was not inferior to enalapril over five years and he reminds the committee that the primary outcome measure was declined in GFR and this was the first study to actually compare that endpoint to an ace inhibitor over five years.
- Henry Tang, Cardiovascular Medical Information Scientist from Astra Zeneca, references the head-to-head comparison mentioned in the review, using two clinical trials to claim one and claim two studies that show that Atacand is superior to losartan in hypertension and that atican is the only ARB with such a comparison and a claiming of the prescribing information. Mr. Tang also spoke about the Scope Trials, because of ethical concern many patients were placed on therapy rather than a placebo. In an article published last year in the Journal of Hypertension in regards to those patients who were not on therapy, entitled The Study on Coniffin and Prognosis in Elderly Scope Outcomes in Patients not receiving add-on Therapy after Randomization. The purpose of this analysis was to discover the confounding effect of the add-on therapy and the results showed that there was a significant drop in blood pressure achieved from atican versus placebo and is also associated with lower risk of major cardiovascular events and 42% reduction lower cardiovascular mortality 29% and lower total mortality of 27%. He then comments on the Charm Program, mentioning that while the other ARB's have shown mixed results in half year trials the Charm Program is a collection of many ARB randomized heart failure controlled clinical trials providing important and additional findings. The Charm had a study generated for its outcome data, which demonstrated the noncommittal use of ace inhibitors and atican and led to a significant reduction in cardiovascular mortality and hospitalization for chronic heart failure patients. Atican was clinically effective in patients on standard therapy for half-aria, ace inhibitors and beta blockers. The study demonstrated that the greatest clinical benefits were achieved with all three of these agents. The Charm Alternative Trial demonstrated that is half-aria patients not able to tolerate any ace inhibitors. Atican significantly reduces upon endpoint of cardiovascular death or hospitalization for heart failure. The Charm Preserve Trial studied patients with ejection fraction greater than 40 and is a population that has not been well studied in the previous clinical trials. While the primary endpoint did not reach statistical significance, the secondary endpoint of reduction in hospitalization for heart failure is clinically and economically important. Moreover, there was a 40% reduction in the risk of developing diabetes mellitus, which is a frequent co-morbidity for heart failure patients. In summary, a supplemental MDSA for use of atican in treatment of heart failure were filed with the FDA in June 2004, because of a clinical significance of the results of the Charm Added Program, the review was released prior to status by the FDA. Astra Zeneca expects approval of a heart failure indication by the first quarter of 2005.

Committee Deliberation and Vote

- Carol Cordy, M.D., asks for clarification regarding a statement made during the discussion on special populations regarding the benefits for heart failure and cardiovascular risk reduction difference in the black population.
- Dr. Furmaga responds referring to the heart failure sum analysis and the Val-Heft Trial. Explaining that within that trial, they looked at the difference in age and other demographics and they found that in the black patients, 7% of their total population, which was 344 patients, there was an increased relative risk of 11% percent of the combined morbidity and mortality outcome. But, within that the competence interval was very wide, .77 to 1.61.,that was for heart failure…The other came dossier of losartan also looked at different demographics and they did find a significant difference in black patients versus non-black patients, which was 6% of their patients population or 532 patients, in the primary endpoint combined cardiovascular morbidity and mortality. This endpoint occurred in 17% of the patients on losartan and 11% of the patients on atenolol. One of the speakers, Laurie McKenna, also

mentioned the FDA indication for patients with hypertension and LVH in the reduction of stroke, but this does not apply to the black patient population.

- Dr. Reese asks Dr. Furmaga whether diuretics were allowed in the losartan and atenolol trial.
- *Tape ends here, Dr. Furmaga's comment was not recorded.*
- Dr. Lessler suggests that it would be easier for the committee to work through each indication individually rather than folding them all into one motion, and working through each indication as listed beginning with hypertension. He also suggests that rather than crafting a motion right away the committee should begin with some discussion and ideas and begin to craft a final motion as the discussion matures.
- Dr. Furmaga leaves the conversation.
- Dr. Cordy comments on the format of the motion template indicating that the only place to add special populations would be in the adverse events.
- Dr. Lessler states that the motion template is simply a recommended form.
- Dr. Cordy comments that this is the first time the committee has had to consider a drug class with a special population which shows a difference and that that population should be listed in the first part of the motion with safety and efficacy.
- Dr. Reese comments to Dr. Cordy that the black population has the same problem with ace inhibitors as they do with ARB's , so they are not equally efficacious in that sub-population so it's a similar problem and doctors need to be aware that that is the case and that an ARB is not good drug for a patient who is black.
- Dr. Lessler comments that the committee can craft a motion that would somehow incorporate that important piece of information. He also asks if anyone has any general observations or comments with respect to high blood pressure and ARB's. There do not seem to be many differences.
- Dr. Reese comments that he does not see a reason to use an ARB as a first line drug if an ace inhibitor can be used. But there are substantial procedure patients who cannot use an ace inhibitor and an ARB in that instance is certainly a reason for hypertension, and then there is no reason to think one is better than the other for the treatment of hypertension according to the data that has been presented to us, they seem to be equally efficacious. But they are second line behind ace inhibitors, because they are very similar to ace inhibitors and ace inhibitors have been out a long time, they are generic drugs, there is a larger body of information regarding their efficacy and safety and they are the standard at this point, ARB's may not be quite there yet, however, they could be a second line drug behind ace inhibitors and position them for hypertension.
- Duane Thurman, Senior Program Manager of the prescription Drug Program, clarifies that the motion template provided in the packets is just a suggested template, and is in no way meant to limit the discretion of the committee in terms of how to make a motion.
- Dr. Lessler asks for further comments in regards to hypertension. There does not seem to be much evidence for difference in respects to declaring one first line and one second line.
- Dr. Bray expresses concern regarding the complexity of the motion and its effect and would like to know what happens for those who have a reasonable indication for these drugs. He states that the committee's task is to be sure they are available and if a motion is made too complex regarding first line or second line it may negatively affect MAA. He feels that the committee should be sure to comment on the safety and efficacy in special populations, either by making some available or not available.
- Dr. Childs responds by telling Dr. Bray that this drug class was originally reviewed by the DUEC and the recommendation was that they would be second line agents and MAA has had them on EPA since 2002 or 2003, so they would use an ace inhibitor first or they would have to be intolerant to an ace inhibitor, a scenario which addresses the cough situation, in which case, a patient could be put on an ARB.
- Dr. Reese comments that the committee should keep the language the same way so ace inhibitors are used as the first line drugs for indication and then we need to talk about which ARB's which are a substantial amount of patients that cannot take ace inhibitors so we need to keep that in mind.
- Dr. White suggests that the committee consider the fact that many people are going to be treated for one indication that will have multiple indications, for example congestive heart failure most if not all will have hypertension as well, although the committee does not deal with combination disease study, he is unsure of how to separate those as these drugs are not made for first line indication.
- Dr. Lessler asks the committee in terms of the role vis-à-vis the PDL is whether or not drugs are effective, equal to look comparatively at efficacy and safety, he does not feel that ARB's are second line in this context. He dopes agree with Dr. White but is not sure that this is the place where specific comments should be made on that as opposed to in the DUEC where all might undertake a review.
- Dr. White comments that the committee is speaking in terms of specific indications.
- Dr. Lessler confirms this.
- Dr. White then comments that if someone has congestive heart failure and hypertension they go to a pharmacy they may not know why the drug is given, it may be given for two or three indications; it becomes very complicated at that point.
- Dr. Lessler comments that in a certain way he is agreeing with Dr. White.

- Dr. White comments that he believes he is disagreeing with himself.
- Dr. Cordy comments that it is a different format and a different committee and in respect to hypertension she asks for clarification on what the committee can say in terms of other drugs not tolerated or infected and if that would keep it on prior authorization. She wonders if the committee is just saying any of these are okay or if it is possible for them to say if other drugs are not tolerated.
- Dr. Childs comments that if the committee can specify that they are second line agents for hypertension MAA can work with that with the same format that they use for putting it on EPA as a second line agent, and if the committee provides other specific indication information it can also be included as part of the coding for the EPA for the individual ARB. SO, if the committee provides a specific recommendation for a second line agent for hypertension then as can work with that.
- Dr. Bray clarifies that if the committee just focuses there comments on the safety and efficacy and special populations that would change what MAA has already decided in the DUEC regarding the second line agent status and the EPA requirement.
- Dr. Childs states that she does not believe it would change it the way it is right now, all ARB's are lumped together and considered second line for hypertension, that is where it was left, it was not broken down by indications other than hypertension but it is possible to do this.
- Dr. Lessler asks the other agencies whether any language used in the motion would recommend that these be available in the case of hypertension reserved as second line agents.
- Dr. Marshall comments that UMP would have no way to reserve them as second line agents.
- Dr. Lessler concludes that it would not affect UMP and is basically the decision around equivalency safety and efficacy.
- Dr. Marshall comments that she is waiting for Duane Thurman's comments on whether this can be done as a committee.
- Dr. Lessler comments that his sense is that as much as he agrees clinically he is not sure it is the purview of this group to comment on this.
- Dr. Marshall responds that as far as she understands it, if they are on the preferred drug list as a drug class they are subject to all the same rules as all the other drug classes would be, so then the discussion might be whether or not they are actually included on the PDL versus whether the committee decides that they are included in the second line. She adds that she will allow Duane Thurman respond to that.
- Dr. Lessler comments that the issue is whether or not it is within the committees purview to comment on if these medications should be used initially or second line with respect to the management of high blood pressure as opposed to commenting on their relative safety and effectiveness for the purposes of agency's making a decision about their placement on the PDL.
- Duane Thurman asks that Dr. Thompson explain how it could potentially interact with drug utilization activities. and comments that if the committee makes the determination that they are on the PDL they are going to be all of the procedural things that accompany being on the PDL , such as the dispense as written override, so it would not leave you commenting on whether it is second line therapy.
- Dr. Thompson replies that he thinks from Dr. Childs' comments that the committee had this on expedited prior authorization, which means a prescriber is never called, there is an automatic system edit that goes in at the pharmacy level. This has worked up to this point with the recommendations from the DUR, previously these are second line agents and the language can be worked with and then submitted to the DUR and they can continue to show you the destinations of the utilizations. Regarding the comment about combinations of CHF and hypertension, fundamentally if the patient needs the medication and it is medically necessary it may sometimes be prior authorized for something.
- Dr. Reese comments that the committee does not need to act on them at all and can leave them in their current position in second line, they are similar to ace inhibitors, and can be bypassed by anyone intolerant using a DAW.
- Dr. Thompson comments that he thinks the challenge is whether they are interchangeable in the drug class, especially as relates to the pharmacy and Senate Bill 6088.
- Dr. Childs comments that if hypertension were treated as other drug classes it would fall under MAA's EPA criteria and would work with the committee's recommendation.
- Dr Lessler asks if there are other points of view. He feels the committee must decide whether they will have a standard motion that comments exclusively on comparative safety and efficacy or whether they expand the motion to include a comment with respect to ARB's being second line agents in the treatment of hypertension.
- Dr. Goo clarifies that if the committee designates the ARB's on the PDL it will then be available as first line.
- Dr. Childs says yes unless she is told it is second line for hypertension.
- Dr. Lessler comments that that addition would be relevant for MAA but not for L&I or UMP.
- Dr. Marshall confirms this statement.
- Dr Lessler says that it does sound like the committee needs to comment on this issue of relative efficacy and safety because of the therapeutic interchange.

- Dr. Cordy requests clarification regarding the expedited prior authorization the (sound of coughing renders speech incomprehensible) the drug class there and pronounce them all equally safe and efficacious, she wonders if there would be a time where they may be interchanged. For example, if a prescription for something that is prior authorization might it be interchanged on the second level.
- Dr. Childs responds that unless MAA is told differently, a DAW will override the EPA and so if a prescriber believe that a patient is intolerant to an ace inhibitor for hypertension the prescriber may write DAW and the patient would then receive the ARB.
- Dr. Lessler adds that the patient would receive the ARB regardless of whether it is on the PDL at that point.
- Dr. Childs confirms that is true.
- Duane Thurman suggests that the committee take a brief break.
- Dr. Lessler announces an eight-minute break.
- Committee reconvenes at 11:00 am.
- Dr. Lessler states that it is clear that if the committee chooses to put forward and vote on a motion that actually specifies by indication that ARB's should be used as a second line agent each agency will deal with that recommendation independently. Another option would be to choose not to put these medications on the PDL at all. He then wonders if Dr. Reese would like to make a motion.
- Dr. Reese requests clarification from Dr. Lessler regarding his comment on ARB's as second line agents, he also comments that he saw no difference of opinion in the groups. He suggests that the committee exclude them from the PDL allowing the provider to tailor the drugs to patients indications.
- Dr. Lessler comments that the committee is more likely to do that but he asks if there are any thoughts on Dr. Reese's suggestion.
- Dr. Bray requests clarification from Dr. Childs, as a follow-through on her suggestion, he wonders, in respect to those physicians who are endorsing, if the committee were to make that decision not to put ARB's on the PDL and the practitioner did not sign DAW what the outcome might be.
- Dr. Childs explains that the DAW opt out will not work and it will be just exactly as it has been for the last two years. There has not been any problem that she is aware of and that everyone gets the ARB if they have tried and failed or are intolerant to an ace inhibitor.
- Dr. Bray wants to identify whether this will generate a lot of paperwork, phone calls and faxes to the doctor is if this is an issue that can be dealt with at the pharmacy level.
- Dr. Childs explains that this happens at the pharmacy with information from the physician.
- Dr. Reese announces that he will go ahead and make the motion and he suggests keeping the ARB's off the PDL adding that there is a drug on the list already that is the preferred first treatment for every indication that an ARB he suggests that they leave the PDL as it now stands.
- Dr. Lessler asks how that would read.
- Dr. Reese replies that basically there is no action to be taken, that the committee would just say they don't need to change the PDL and a vote can be taken to prevent them form being added to the list or the committee decline to vote and state that the ARB's are not on the list.
- Dr. Lessler says ARB's will not be added to the PDL and that is the motion.
- Dr. Thompson comments that a vote would be appropriate.
- Dr. Lessler asks Dr. Reese if his previous comments was accurate.
- Dr. Reese announces that his motion is not to put the ARB's on the PDL.
- Dr. Marshall asks Dr. Reese to read the motion as it is displayed on the projector screen.

> **Dr. Reese:** I move that the A2RA drug class should not be added to the Washington Preferred Drug List.
> **Second:** Dr. Goo
> **Vote:** Motion Passes

- Dr. Cordy suggests that a synopsis of the rationale for keeping this medication off the PDL be composed and if people choose to prescribe these drugs some rationale for which ones are indicated is then available to read. This is to be sure that the committee is providing some education. She feels the committee ought to be educating pharmacists and prescribers.
- Duane Thurman comments that the appropriate way to do that would be as a portion of the discussion combined with the vote taken and so if that is to be kept on the record it can be put into the transcript and onto the website.
- Dr. Cordy comments that the synopsis would be a summary of the different indications and the studies.
- Dr. Lessler asks if she is volunteering.
- Dr. Cordy then amends that is should be a short summary that would anticipate a prescriber interested in prescribing this drug, this prescriber can then go to the website and find out why it was not on the preferred list and have some direction as to which of these medications would be best.
- Dr. Lessler clarifies that they can prescribe the drug.

- Dr. Cordy responds that with this piece of information they would have some direction as to which is the better drug.
- Duane Thurman explains that as staff he does not want to come up with the committee's rationale, so he would require some overall principles and then provide some informational research to include in the synopsis. He also adds that it would be helpful to have a statement from someone on the committee to say what the issue was and why the motion was made, he explains that the staff would need some direction from the committee.
- Dr Lessler comments that he will take his prerogative as committee chair and say that this is not a project which the committee will pursue, the committee's motion and decision have been made and the committee will move on to the next item on the agenda. That item would be the discussion on antidepressants. Dr. Helfand will join via teleconference and the floor will be opened to additional stakeholder input. The committee has an excellent set of complete transcripts from the last discussion on Second Generation Antidepressants. Once Dr. Helfand is available by phone any members of the committee are welcome to ask questions of him at this time in terms of clarifying the evidence based reports.

2nd Generation Antidepressants

Continuation of the discussion at the December 15, 2004 P&T Committee Meeting

- Dr. Lessler addresses Dr. Helfand explaining that the committee is continuing their conversation from the previous meeting in regards to Second Generation Antidepressants. He opens the floor to the committee for questions or points of clarification from Dr. Helfand with respect to the evidence based report. HE also introduced Dick Mioshi, Pharm.D, a consulting expert in the area of psychiatric medications, who was present during the latest discussion on second generation antidepressants.
- Dr. Reese asks for clarification regarding the fact that nefazodone has caused several idiosyncratic fatal episodes of hepatic toxicity and hepatic failure.
- Dr. Helfand confirms this statement.
- Dr. Reese asks if that situation is unlike the other drugs, whether SSRI's or other antidepressants, and asks if any other drug has received similar reports.
- Dr. Helfand responds that he is not sure.
- Dr. Reese adds that he was not aware of any drugs that were reported with the frequency that nefazodone has been reported but he was wondering if Dr. Helfand was aware of any.
- Dr. Helfand states that he is not aware of any.
- Dr. Ballasiotes asks if Dr. Helfand can comment on the problem with regards to liver toxicity with nefazodone and if it is serious or is it less than serious but does need to be monitored.
- Dr. Helfand does not feel he can provide more information than that can be found on page 64 of the report, he also references the Chase reports that show an increased risk in liver toxicity but that that cannot be translated into a percentage of risk as there is no denominator. All that can be said on the subject is reiteration of Dr. Reese's statement that there is a higher frequency of case reports with nefazodone that is not seen with the rest of the drugs in the class, but whether that is a one in a million, hundred or thousand risk he does not know.
- Dr. White asks if the discussion is only regarding liver failure.
- Dr. Helfand clarifies that he is speaking of cases of clinical liver failure and cannot comment any further or cover any more information than what can be found in the report or in Dr. Reese's comment said. He does feel comfortable saying that in the text of the paper a reference is made to a decision that somebody else made, such as nefazodone in Canada was drawn but OHSU does not study those kinds of decisions to see how they weigh the risks and benefits. He adds that something that is not a matter of the evidence is more the matter of the decision-making and how someone weighs the information.
- Dr. Mioshi comments that there were a number of cases in Australia and some in Canada, Europe took it off the market a couple of years ago and Canada was the last. There were impassioned pleas by many tertiary care people who treat the worst cases not to take nefazodone off anything because of its unique profile. Also, there is no real patterns showing why these people actually had failure it was purely idiosyncratic.
- Dr. Helfand comments that he does not feel it would be going too far to look at the black box warning from the FDA, as it provides the FDA's assessment of the risk, however, OHSU does not have the same ability to estimate as does the FDA. The black box warning says everything, "cases of life threatening hepatic failure have been reported and patients treated with serzone, the reported rate in the US is approximately one case of liver failure resulting in death or transplant for 250-300, 000 patient years of serzone treatment, the total patient is a summation of each patients duration of exposure expressed in years." That is the information they provide to prescribers.
- Dr. Lessler announces that the committee will now open the floor to stakeholder input; he asks that if there are several speakers speaking on behalf of the same medication that they somehow coordinate or recognize that

someone has already made your point. Therefore, we can get through the comments more efficiently, also if anyone has evidence that they would like considered it does need to be submitted to OHSU, we are not able to consider new evidence that is presented here by a stakeholder.

- Dr. Graham requests that any stakeholders who spoke to a specific drug during the last discussion of Second Generation Antidepressant please know that we have your comments recorded in the transcriptions and to refrain from commenting unless new evidence will be presented.
- Dr. Lessler reiterates Dr. Graham's request.

Stakeholder Input

- Daniel Wanwig, M.D., emphasizes Zoloft and sertraline, commenting that the SSRI's are the mainstay of treating depression. Sertraline has widest range of indication of any SSRI, and has been tested and is safe in co-morbid psychiatric conditions such as alcoholism, personality disorders and Parkinsonism. Another important point is its safety and efficacy in the aging population, he has had a great deal of good acting experience in that population, and adds that it was tested in a series of 700 patients in the 60 year old and older group, and in that series the individuals did not have any higher drop out rate than any other individuals. Another point in his practice is that older people have lots of cardiac problems, sertraline was tested in a series of patients with acute coronary syndromes. Both acute MI's and unstable angina, these patients are approximately 300 in total and were randomly assigned to either receive sertraline or placebo and all of the ejection fractions were measured again at 16 and 24 weeks, there was no significant difference in the cardiac performance of the individuals who were treated with sertraline and the ones who received the placebo. This is a very solid piece of evidence suggesting the safety of this drug in this population. The final point he mentions is that sertraline has a very favorable Cytochrome P450 profile, it basically is not exceeded by any drug and in particular that most of the psychiatric medications and cardiac medications are metabolized through that route as well as many antibiotics and similar benzodiazepines.
- Lenora Warden, a psychiatric patient, who spoke to the benefits of Celexa at the last meeting, testifies that as a result of your comments on reading she has done she would offer Celexa to the generic but it is not the same, her racing thoughts have returned, some of her sleeplessness and her mild depression as well. Speaking for psychiatric patients she comments that they still have to deal with living their daily lives, trying to get used to new medications or different kinds of symptomatic changes for medications, but, as they do this it alters some of the quality of our lives. She states that she will continue to stay on her generic medication and try to work with the different effects she is experiencing to see if she can challenge some of this, and hopes that the committee is looking to her safety.
- George McKay, another psychiatric patient, was first diagnosed at the age of 27 with major depression and the drug he'd like to address is the generic to Paxil, which he admits he cannot pronounce. He states that when he takes this generic form he experiences far more anxiety and fear and he seems to stay inside the house. His mind races and he stops taking care of himself as far as bathing and grooming, he admits that there are times when he is afraid to go outside to empty the garbage. This usually leads to a meeting with Social Security and Disability and he does not always get his medication paid for which then causes him to call the crisis line and from there going to the hospital for a week until they stabilize him as much as they can, the concentration and the balance does not occur immediately, and being on medication limits his freedom. Also, without stabilization he feels he cannot hold a job, he has lost his family and been hospitalized 29 times since the age of 27, he is fifty-one now, he has been in jail and been homeless, just as a result of running out of medication.
- Dr. Sharon Romm, an associate professor at the University of Washington, attempts to speak to sertraline.
- Dr. Graham interrupts Dr. Romm to ask her if the testimony she will give today will provide new information that was not heard during her testimony at the last meeting.
- Dr. Romm responds that the information is the same information that she presented at the last meeting.
- Dr. Graham replied that her comments had been recorded in the meeting transcripts and that her testimony would not be necessary.
- Dr. Robert Povian, Senior Director with Pfizer Medical Division, comments that he did not speak at the last meeting and that what he was about to present was new information, he also comments that he hopes that during public meetings all people will be allowed to speak. He goes on to say that the University of North Carolina first prepared the report that as presented, not the Oregon Health Sciences University. He adds that on January 14 there was a solicitation by the Center for Evidence based policy research for a new set of key questions for the antidepressant report, although the key questions on the report were only presented in final draft, it was presented in the first week of November. One of the key questions that has significant changes is the first one, which addresses and asks what the differences are between these agents not only in efficacy but in effectiveness, what are the outcomes of this report in the totality. The reason being, is that effectiveness is very different from efficacy, most likely we anticipate a report coming out within the next two months, you will be sitting around and making another decision in two months based on a changing of the key questions that are coming from then University of North Carolina. While we appreciate the opportunity as pharmacists and as stakeholders to comment on these reports and that the center for evidence based practice research has allowed stakeholders and peer reviewers to comment on

these reports they have failed to disclose those commentaries in their reports. They have also failed to say whether they included those commentaries or not in those reports, not only have they failed, Pfizer submitted a 8 page document to them on the antidepressant report, and not a single point was inserted into the report, and they failed to disclose why the information was not valid enough to be included. He addresses the P&T Committee and Medicaid specifically when he says that both of these groups are touted as partners for the center for evidence based policy, he asks that they please be aware of this situation and ask the center why they do not disclose all of the public information that is garnered from the both stakeholders and peer reviewers.

- Larry Cohen, M.D., who spoke at the last meeting, professor and chair of the department of pharmacotherapy at the University of Washington, announces that a handout that was circulated earlier in the morning on which he would like to comment. Something that has been used as a principle source of information and something that the committee uses in their reviews with the OHSU evidence based medical document, which does not have to do with validity of the document. What he found that was of note was the paragraph which shows the difference between efficacy and effectiveness and very important for people to comprehend, what is says is: our evaluation is based on independent scientific review of the evidence on the effectiveness, safety, and adverse events of antidepressant. This is the consumer reports statement " a team of physician and researchers at the OHSU evidence based practice center conducted analysis as part of the drug effectiveness review project. This is a one o a kind twelve state initiative to evaluate the comparative effectiveness not efficacy, but, effectiveness of safety of hundreds of prescription medications and the reason I think it is important is that many people depend on the kind of information that is in consumer reports and they talk about things like what is the best buy of drugs, and they talk about least expensive products that are listed here. He also references the comments heard by the consumer, Lenora, who has had in terms of efficacy all of these drugs in clinical trials may be shown to be the same in efficacy and effectiveness is a different entity. When you give these drugs to real people whoa re not in a controlled clinical trial setting, effectiveness is a very different concept and that should be taken into consideration. The decision of what is available in Lenora's case having to do with the trade name product and the generic, all generic products are not the same. Changing patients from one generic product to another within a class occurs frequently in the community based on where somebody gets their drugs and prescriptions filled and whatever is under a contract that changes from year to year, can have a big impact on individuals who are treated like Lenora.
- Peter Lukavitch, Executive Director of Partners in Crisis, which is a criminal justice stakeholder coalition of prosecutors, sheriffs, police chiefs, judges, treatment providers and consumers, as well as the public defense bar. He explains that he is a former criminal defense attorney and a municipal court judge and has now been working with this coalition regarding the way the treatment of the mentally ill in the criminal justice system. As a result of this experience I can share with you that the rate of mental illness in our state prisons and jails throughout the U.S. is about 16 percent, or at least three times the rate of the general population. And that at least three quarters of the people with mental illnesses who are incarcerated have a co-occurring substance abuse disorder. He shares this information with the committee from the criminal justice mental health consensus report that was commissioned and released in about 2003, I want to set the stage in respect to that particular population, whereas an untrained clinician or prescriber or doctor before you today would characterize that as a class or a sub class of people. He expresses deep concern as do the members of the coalition that the evidence based practice research that you are relying upon has not taken into account that very unique and different class of patients. The reason why it is important is because the studies that the committee is relying upon, the controlled clinical trials where issues of co-morbidity which are not diagnosed well in our prisons and our jails, the compliance of which is dogged in the clinical trials. He assures the committee that in a prison and jail situation or upon release the patients are not as compliant as one would like them to be, and finally the environmental concerns to the environment in which you are conducting the trial. He then suggests that there has been no trial for this particular class and the reason why that's important is because it is not done that pristine or comfortable clinical situation. Treating the mentally ill is considerably different than doing that in a traditional clinical setting. He asks that the committee, rather than ultimately move or consider this class of medications for assignment to the PDL, or individual drugs within the PDL, as was done with the previous class, is to put it on hold for a while and consider whether it is better to commission that particular course of study either through the evidence based practice center or on an individual basis in this state. Because these individuals travel between institutions they become Medicaid eligible in one sense, then they go to a city jail, then they lose their Medicaid Eligibility they would then transfer to a county jail because their seriousness of offence was beginning to increase ultimately for some reason they find themselves in the federal detention center at SeaTac, and then subsequently because they have been released or whatever the procedures have occurred they find themselves in the state DOC or prison system. In addition to the fact that we have not reviewed the class and we haven't concerned ourselves with the environmental consequences of the effectiveness of treatment within that class of people, there is no longer a prison system that communicates,. He acknowledges Dr. Thompson because he has assured him that this problem will be solved. But it is extremely important for the committee to know that as you go through the decision making process that the jail prison populations do not communicate with each other as health care providers, so the frequent flyer that goes from city to state to federal to county has no assurances of the refill issue and there would be problems concerning DAW and

whether it was prescribed before and what the records were so that we could continue the course of treatment, so because of those reasons he asks that the committee delay any decisions on this and to seriously consider evaluation this population or class separately before you render your final opinion.

- Dr Lessler announces that concludes stakeholder comment and the floor is now open it up to discussion amongst P&T Committee.

Committee Deliberation and Vote

- Dr. Lessler comments that one aspect of the discussion last time was the idea of trying to talk about the indications in a collective sense and attempt to fashion a motion in that way. Lets try to get some discussion and not begin with a motion, is there anyone with any comments or observations people might make about the antidepressants generally or thoughts people think would be helpful toward moving us toward some sort of consensus.
- Dr. Goo clarifies that the committee's discussion is in reference to new starts.
- Dr. Lessler confirms this and adds that this means specifically someone who is currently on an antidepressant treatment that would not be therapeutically interchanged.
- Dr. Reese asks for clarification on the idea that there are AB rated generics on every drug in all classes except for esotalopram.
- Murmured discussion among the committee and workgroup.
- Dr. Childs comments that three do not have generics, specifying that is the second one on the list which is the generic for Lexapro, the fourth one the list of SSRI's, the generic for Zoloft, Sertraline and the other is venlafaxine which is the generic for Effexor.
- Dr. Lessler mentions nefazodone.
- Dr. Reese comments that the brand name was withdrawn.
- Dr. Lessler comments that it strikes him, conceptually thinking, that the committee would want to assure some mix of medications to allow initial tailoring, although even with the best initial clinical judgment, a large proportion, as much as 40 percent ultimately need to try and second the agent and then possibly want to see some sort of mix with respect to mechanism of action in some sense.
- Dr. Ballasiotes comments that he deals extensively with antidepressants and deals with co-morbidity and does a lot of work with the jail population and he understands that it is very difficult to find one drug, an antidepressant that is going to fit the patient. He explains that he often has to change medications on the patient to provide them some relief from both the depression and their anxiety, so he thinks that this is going to be a problem in just categorizing the drug or what specific drug to make available.
- Dr. Graham comments that DAW is available for endorsing practitioner and he reminds the committee that this discussion is focused only on first starts.
- Dr. Bray offers to attempt to piece together a frame work, not a motion, in regards to how he sees this category of drugs and how he thinks the committee could approach the situation. He states that he agrees with what was said and with such a small array of options, selections can be made choices on uniqueness of medication, as well as safety. When safety comes up, given the evidence presented, the committee must say in the pediatric population that fluoxetine would be included when it comes to the unique pharmacokinetics of some of these drugs. He also recommends that venlafaxine would be an important drug to have on the list, buproprion should be on the list due to its unique nature regarding side effects, and there is evidence that mirtazapine separates itself because of the issues of rapid onset and also the issues of weight gain, which is important in some depressed patients. Nefazodone is not unique in its benefit and there are concerns regarding safety that have been brought up. Then the selection of drugs remaining is a group where there are probably more similarities that differences and that would be citalopram, esotalopram, sertraline and paroxetine. And because of the other pharmacokinetic uniqueness of fluoxetine and venlafaxine they should not be substituted and it can be argued that all these individual drugs mentioned, because of their uniqueness, should not be substituted.
- Dr. Reese states that he thinks this is a good way to think about it. He believes that there should be a broad number of drugs and that almost all mentioned are generic except for a few exceptions, Venlafaxine is one and Sertraline, although that will be generic shortly. He suggests adding all of the generics of every drug, plus venlafaxine and sertraline cannot really be substituted the only thing, he feels that Lexapro should be left out of the recommendation. Nefazodone, as well because of safety concerns, so just leave those two out and put everything else in the recommendation. This will cover a broad gamut of drugs AB rated generic that can be substituted for the brand name product even in products that have a brand name, batch to bath there are variations in product. AB rated generic as the drug substituted should provide an idea that it is the same drug at the same dose as the one for which you are substituting it. However, a very wide group of drugs in this category is important, because if you change drugs in somebody's system and you cause a depression it is a disaster.
- Dr. Ballasiotes disagrees with leaving nefazodone off the list, he feels it is a very good anxiolitic drug, especially with alcoholics, whereas other antidepressant does not work as well as far as containing anxiety. It also

works with respect to sexual dysfunction as an alternate for people who have experience sexual dysfunction on the regular SSRI's, it also helps with regards to sleep and recalibrating the sleep cycle.

- Dr. Bray states that he would decline to argue the things that Dr. Ballasiotes is pointing out with nefazodone, but he would argue that none of those issues mentioned can be dealt with either other drugs within the class or other drugs outside the class, and his concern remains that it cannot be said that it is safe because of those idiosyncratic liver-failure reactions.
- Dr. Graham comments that nefazodone does not have any published evidence.
- Dr. Ballasiotes explains that nefazodone works as anxiolitic because it works to block the 5HT2 receptor and because we know that some SSRI's do cause some anxiety in some people, it better to go slower when beginning.
- Dr. Graham asks Dr. Ballasiotes if he would consider that as a new start drug.
- Dr. Ballasiotes says no, he would not.
- Dr. Graham reminds him that the committee is referring only to new start drugs.
- Dr. Goo asks Dr. Mioshi to comment on the clinical safety or drug interactions as far as venlafaxine. Does he feel clinically that it provides a unique pharmacokinetic profile that is clinically important.
- Dr. Mioshi replies that venlafaxine has very few drug interactions and citalopram, esotalopram, and sertraline. The only thing that makes it different is this dual action. This would be the place where we would go when one or two SSRI' were not working. It's the next step down, the other point that Dr. Ballasiotes brought up was sexual dysfunction when Prozac first came out and prescribers were looking at 15 percent and now are looking at 35 to 50 percent. If research was done on the reason why people stop their antidepressant, sexual dysfunction is a huge number and so it would be nice to have drugs that don't have that same mechanism, which is a decrease in serotonin which causes that issue. That means the use of nefazodone, buproprion and possibly some soft stuff about mirtazapine.
- Dr. Ballasiotes explains that venlafaxine has a short half-life, and there is not a high incidence of withdrawal on that particular pharmacokinetics of that drug, prescribers also do not always do a very good job of patient education. It is also the patient's job to help them come off that drug or when they are switched over and that scares people when they don't know what's happening to them.
- Dr. Lessler asks if Patti Varley has a comment as this is her field as well.
- Patty Varley, ARNP, comments that when considering new starts she agrees with what Dr. Mioshi said, the prescriber starts with something and then finds the individual has certain side effects or a lack of efficacy from one drug and it is difficult to find a good fit. During the last discussion on this topic the same point was raised, that it was difficult to find one drug that fit all, She believes that this is a situation in which having flexibility within a class is an important thing and because there are weaknesses across the board with all of these drugs, within individuals and within medications themselves.
- Dr. Lessler agrees with the point of flexibility and providing more than three alternatives, but as there develops talk of some of the common side effects, the sexual side effects and about new starts and then maybe the ability to go to a second agent if the initial therapy did not work due to side effects, he wonders whether that can be done with fewer drugs than d. Bray had listed for initial starts and maybe initial change, understanding that if a patient failed two medications that were actually on the PDL it would still be possible to access one of the others either through request or by writing DAW.
- Dr. Bray suggests that the committee be aware of new starts from the standpoint of insurance coverage and what would be considered the first time that person has been started on an antidepressant with that coverage. Many patients come in and are a new patient to the doctor or a new pt to the insurance coverage but they often times are not a new patient when it comes to the diagnosis of depression. They may come with history of being on a specific drug and the experience of it working for them or not working for them due to side effect profiles. So, it might be seen as a second line kind of thing or it may be seen as a new start for the insurance purposes, but the patient comes with a history that needs to be considered by prescribers when they begin drug therapy. He explains that this is the reason that he suggested more of these unique drugs for the list.
- Dr. Thompson comments that as far as refills, MAA will work with the stakeholder group to be fairly broad and generous with the definition of a refill. The challenge is when patients come from a state institutions; a hospital, prison system, county jail, there should be some provider education regarding the process of patient refills and he explains that he will be very generous as he doe not want to cause another depressive issue or something even worse. MAA has been allowing expedited prior authorization and trusting the client when they explain that they have tried and failed a specific drug or they don't like the purple pill because of a color agent they are allergic to. Dr. Thompson explains that 8 percent of our overall budget goes to brand when there are generics available, and quite often it is just that conversation between the pharmacist and the client and the expedited prior authorization. He does think that the group has some work to define refill under Senate Bill 6088 and there is also a huge amount a work with all the advocates on how do we make sure we don't have unintended consequences as it relates to these drugs.
- Dr. Marshall comments that the refills are defined as a continuation of therapy which includes adjustments in dose so if they are on one antidepressant and they need to increase the dose, which is considered a refill or continuation

of therapy. And she believes that the intent is that the refill is defined at the patient level not according to who is paying for it or who may have prescribed it. So, if they are on a drug from a prior prescriber or a prior plan that would be considered a refill also because it is continuing their therapy.

- Dr. Lessler asks if that would be the case with MAA
- Dr. Thompson sys that yes and the challenge will be how to identify that on the prescription and that is what is being discussed with stakeholder group. He explains that it may be as simple as reeducating the provider population.
- Dr. Marshall comments that the challenge is for those enrollees that are already in our plan that can identify electronically those refills. As for those enrollees that are new to the plan they would hit up against an edit as being a new start and they would have to get the prior authorization somehow. The patient could tell the pharmacist that they have been on this medication before and it's just a phone call to Express Scripts to load the prior authorization. However, the next time our system would catch it and it would fall under the refill.
- Dr. Fisher states that she thinks the problem is that everyone was defining new starts as a person newly on medication and the problem has been transmitting that information.
- Dr. Thompson comments that he has asked the stakeholder group to make comments because of the idea of refill in continuation - does that mean they have to go from 1 month, 2 month, 3 month, 4 month, within these classes and other classes there are interruptions in therapy that occur for a number of different reasons and that will be some work that the stakeholder group will give to staff. Would interruption of one month still be considered a refill.
- Dr. Graham again comments that the DAW is still available at any time a provider feels the patient needs a specific drug whether it is a new start, a refill, or whatever. That information will be sent out to providers as not everyone knows about it, that is part of the PDP's educational programs and there is good participation among most of the people who do prescribe these, such as family physicians and internists. There is still some work to be done with the psychiatric community but otherwise people are beginning to understand the program.
- Patti Varley comments that that would apply not just amongst agents but within the agent for brand versus generic that if the committee felt that a patient had a history of previous trials that it could also be done for a brand versus generic.
- Dr. Graham comments that he understands that Dr. Thompson has 8 percent of the budget right now for this reason.
- Dr. Lessler addresses Dr. Bray and asks if those comments addressed his concerns about people might come to a provider newly on Medicaid who have previously been on some medication that has been effective. That would not be considered a new start, and so it is difficult to say what would be considered a new start, therefore, it might be an idea to have a limited number of medications on the PDL albeit several so there would be options and so forth.
- Dr. Bray says yes.
- Dr. Lessler asks Dr. Ballasiotes if his questions have been sufficiently answered.
- Dr. Ballasiotes says yes.
- Dr. Lessler suggests that the committee look at Dr. Bray's frame work which is very helpful, and he assumes that all agreed on what a first start is and what continuation means and that the way the committee might consider going would be amongst pure SSRI's that would require that fluoxetine be available for the reasons stated for the pediatric population and that there be at least one or two other SSRI's available and then within the other, making buproprion available on the PDL but not the others. Understanding that if somebody had responded and presented themselves before a provider on those medications would they would receive them because that would be a continuation if a new start that had failed any one of these SSRI's or buproprion. This addresses some of the issues around sexual side effects that one of these others that would be nefazodone, venlafaxine or mirtazapine would be available by writing DAW or by requesting them through prior authorization.
- Dr. Reese expresses concern that that is too restrictive and that for the elderly patient who is low in weight mirtazapine is his first choice as they are starving. He feels the committee should have a broader number of drugs available so they can apply them to patients that need them. He explains that eh does not feel they need to have as many options as possible, but within reason. Although, he does not feel that nefazodone should be on first line because he thinks the prescriber should be able to write DAW for the patients in special circumstances. He also does not want to encourage its use as he does not want to kill a patient and that he would not prescribe that drug himself. He also does not see a reason to put escitalopram on the list as isomer is its generic. There are reasons to select specific drugs for first starts, there is good data for subgroups and there is need for a broad net, and we should not force the provider to go through something that is not going to work before they can get to the drugs that will work, normally he explains he would want a very narrow choice and he explains that this is very difficult.
- Dr. Graham repeats that there is the option of writing DAW for those special patients, he feels the committee is focusing on the five percent or less of the patients for a program that is for 95 percent of the patients. He explains that if the committee does decide on a narrow recommendation the endorsing providers have the full array of drugs at their disposal.
- Dr. Marshall suggests that people have in mind the idea of DAWQ when it was first introduced and sued mostly for targeting brand name drugs, however, it is possible to write a prescription for a generic drug and write DAW and a

pharmacist is required by law to dispense that drug as written, so if generic is not preferred it would still be eligible for the dispensed as written opt out just like any of the brand name drugs that are not preferred.

- Dr. Goo addresses Dr. Mioshi with a question regarding SSRI first starts and how reasonable it might be to have a choice between citalopram and fluoxetine, with the exclusion of fluvoxamine.
- Dr. Mioshi states that is a reasonable way to look at it, the longest half life and the second longest half life, the 2nd longest half life citalopram has one or two interactions while fluoxetine has the chance of having a current number of interactions, look at the list of interactions, there are a myriad of interactions that can occur, those are outliers once again.
- Dr. Thompson comments that the drug-drug interaction are hard wired into all pharmacy systems, if there is one, albeit they are at 50% override in the pharmacy system, or more, there would be a call that would be initiated from the pharmacist to the physician, that is how it is supposed to work within the system, so that drug-drug interaction is hard wired into all pharmacy systems.
- Dr. Lessler suggests that if there are no more comments the committee might attempt a motion.
- Dr. Cordy asks if the committee is interested in removing the generics form the PDL.
- Dr. Lessler answers that the committee is looking to make a recommendation regarding these medicines for the PDL
- Dr. Cordy comments that just because they are generics that doesn't automatically pay them to the PDL.
- Dr. Lessler comments that that is what he was hearing before and maybe the committee would want to comment on that.
- Dr. Marshall gives an example from the beta blocker class- explaining to the committee that they basically stated that for different indications, numerous drugs were equally safe and efficacious and the state then based their decision on the cost with all those drugs that were considered similar. Not necessarily all the generics were added to the list, again that is not a decision for the committee to make, if a certain drug chemical should be on the list, then that must be stated or if it will read three out of five or whatever need to be on the list or state that all generics are equally safe or should be on the list. The committee does not need to determine which generics aren't on the list and which are unless there is a clinical reason to do so.
- Dr. Thompson refers to the pharmacy report on rx.wa.gov where there is a financial calculation process, typically when the drug classes include a broad array of generics it is not then the state's experience or best interest to be exclusive. Usually there are 2, 3, 4, 5, or 6 or many drugs when there are generics available. He thinks it is more based on clinical and on efficacy and if there is effectiveness also then that can be worked in and that has been done on every class and the PDL is not a restrictive preferred drug list.
- Patti Varley comments that the committee's job is to select out of a group what medications are equally safe and efficacious.
- Dr. Lessler comments that in general that is true although the committee has learned that there is some latitude there, for example, certain drugs can be recommended that they must be made available as preferred.
- Patti Varley replies that she believes that when they do that it is for patient safety reasons or for effectiveness reasons not for cost reasons.
- Dr. Lessler asks for comments from the committee on broader versus less broad options, he also voices concern regarding therapeutic interchange. He feels comfortable with this idea for the most part, but he also feels that he would not feel so comfortable deciding that any drug not on the PDL for this indication is therapeutically interchangeable. With a narrow choice of drugs there is the possibility to use the DAW option, however, if for some reason that DAW is not placed on the prescription then there is a chance that the non preferred drug prescribed will be interchanged, whereas if there was a broad array of drugs this might not happen.
- Dr. Marshall comments that with the mirtazapine there is a different drug class not for the entire class but a particular drug could be available for a certain sub class and if that would be appropriate too for those types and that would give the agencies the latitude to give the people who really needed the medication without going through the full prior authorization process and still allowing the providers to have choice. For instance, if the recommended Coreg is available as a beta blocker for patients with heart failure, not necessarily that it be available for first line agents in the treatment of hypertension. So as an example, if the committee stated that mirtazapine should be available for an elderly population and that would give Medicaid the ability to put an expedited prior authorization if that was necessary.
- Patti Varley provides the pediatric example of the skinny, non-sleeping depressed kid in which she would also choose mirtazapine.
- Dr. Reese suggests that they just have every generic on the PDL as that was what Massachusetts did and it seemed like a very smart idea and an easy way to start if they want to have a narrow broad way of choices, that way every generic is automatically on the PDL and there can be further discussion about the ones that are not generic and whether there is a special need for them to be first line drugs.
- Dr. Lessler if you don't write DAW *(interrupted by unidentified speaker)*
- *(unidentified speaker is inaudible)*

- Duane Thurman comments that there is a blurred line between when the committee is involved in a drug utilization action and when they are involved in P&T Committee work and he wants to emphasize that it is not about cost or when something might become generic in the next six months or two months, the point is what does the evidence show. He instructs the committee to keep in mind that as the drugs classes are implemented there will be input available from a utilization standpoint. What is needed from the committee is a recommendation made from the available evidence and if that recommendation will allow us to substitute a drug or not and if there is a situation in which there is a possibility that would allow a drug to be improperly substituted the committee should err on the opposite side of that.
- Dr. Cordy states that the committee collectively does not believe the evidence as at the end of the presentation and report it says all the drugs are basically the same and we are saying that they are not.
- Duane Thurman comments that he believes that is the issue before the committee.
- Dr. Lessler asks Dr. Reese if he wants to attempt to craft a motion and specify the medications as opposed to saying generics or non-generics.
- Dr. Reese states, "after considering the evidence of safety, efficacy and special populations for the treatment of depression along with manic depressive disorder, dysthmia, bipolar disorder, general anxiety disorder, compulsive disorder, panic disorder, post-traumatic disorder and premenstrual dysphoric disorder I move that citalopram fluoxetine sertraline fluvoxamine paroxetine vertazipine venlafaxine and buproprion are safe and effective no single second generation antidepressant is actually fewer adverse events in special populations." Now we have to talk about therapeutic interchange. "These drugs can be subject to therapeutic interchange in the Washington Preferred Drug List for the treatment of depression as first starts." The two drugs I am leaving off the list are escitalopram and nefazodone.
- Janet Kelly, Pharm.D, comments that Dr. Reese just said that they can be substituted so that when you write a prescription is written for mirtazapine they can substitute something else, she recommends that it read "they cannot be substituted."
- Dr. Reese comments that he is trying to craft it to the template.
- Dr. Lessler offers " that these should be available and that they cannot be substituted as first starts."
- Dr. Reese offers "these drugs should be available and cannot subject to therapeutic interchange in the Washington preferred drug list for the treatment of Depression and all the laundry list of similar or related conditions".
- Dr. Marshall edits the motion template that is projected onto the screen to reflect the Dr. Reese's proposed changes.
- Dr. Cordy comments that she still does not quite understand why buproprion is included as treatment for anxiety disorders because it is not.
- Dr. Lessler responds that he think what the committee is trying to do is look at these conditions in a global sense.
- Dr. Reese suggests that he just say "major depressive disorder" and then let the providers figure out all the rest. He also suggests leaving off fluvoxamine as it is not indicated for major depressive disorder. "After considering the evidence of safety efficacy and special populations for the treatment of major depressive disorder I move that citalopram, fluoxetine, sertraline, paroxetine, mirtazapine, dimafaxin, buproprion are safe and effective no single second generation antidepressant is associated with fewer adverse events in special populations. These drugs cannot be subject to therapeutic interchange in the Washington PDL for the treatment of major depressive disorder.
- Dr. Goo suggests that it might be cleaner to say that those drugs listed are on the Washington State PDL and just say that those are the preferred agents and they are for first line.
- Dr. Graham makes a point of clarification regarding his preference that Dr. Reese leaves it the way it is, as that is the way the committee has done them until now. Unless there is one drug that should specifically be placed on the PDL.
- Dr. Reese mentions venlafaxine and sertraline as two drugs which are not available in generic form at this time.
- Dr. Graham states that they can be put on at that time, if there is a need to have venlafaxine on there right now.
- Dr. Goo states that he was going to deal with the drug list later on and just wanted to get the wording first.
- Dr. Marshall clarifies that the committee is stating that these should be available and then asks what the committee wants to do about the drugs that are not listed. She suggests that the committee can list them all as being equally safe and effective and then list this list here as those that should not be interchanged. For example, if the motion should read that all the SSRI's are safe and effective and can be interchanged with the ones that are not listed and someone was prescribed escitalopram then the pharmacist could give citalopram or one of these others in its place. As it reads right now all of the drugs that are not listed here would not be subject to therapeutic interchange. This says that they are not safe and effective.
- Dr. Lessler interjects that the committee is not saying that these drugs are not safe and effective.
- Dr. Marshall replies that the committee is not saying they are not safe and effective but the motion does not list them as being similar in safety and efficacy as the others.
- Dr. Graham suggests the committee keep in mind some of their previous motions made for drug classes where they listed all the drugs which they felt were safe and effective and then specified that particular drugs should be on the PDL.

- Dr. Reese comments that he would hate to have these drugs therapeutically interchanged without the prescriber knowing even for the medications that are not on the list there may be things that the committee is unaware of and that is why the provider prescribed that particular drug or they may have been on it before and the records are not in, many reasons, but he does not feel comfortable therapeutically interchanging the drugs that are not on the list. They have to call the provider and tell them they cannot prescribe Lexapro, they must prescribe something else if this is a first start.
- Dr. Graham reminds the committee of the time they reviewed statins and the committee specifically left one drug off the list, he asks Dr. Reese if he is excluding two of the drugs because he feels thy are not safe and effective.
- Dr. Reese comments that one drug is not safe and the other is isomer, which is on the primary.
- Dr. Lessler suggests that the other reason to leave a drug off the list is because they do not believe it is therapeutically interchangeable.
- Dr. Graham suggests that that could be better stated in another way.
- Jason Iltz, Pharm D, suggests the committee handle this in two separate instances, first saying which medications are safe and effective, once we come to that point we can make a recommendation to the committee to say now we would like to recommend that these meds be considered for inclusion to the PDL out of the medications we have listed as being safe and efficacious. To almost handle it in two separate scenarios.
- Dr. Fisher asks if the committee is trying to say that this is recommended list of medications and that nefazodone is not considered to be safe and effective but that the others should not be therapeutically interchanged.
- Dr. Iltz confirms her statement and then suggests that the committee make certain recommendations of drugs that should be added to the PDL in consideration of first starts.
- Dr. Fisher suggests that if the committee wants these drugs on the PDL because they are safe and effective then you want to list them and say they are not to be therapeutically interchanged.
- Patti Varley questions the selection of certain drugs which have been placed on the list rather than off, and comments that the committee has clearly spoken of nefazodone and the liver problems but she is unclear as to why the other drugs are being excluded.
- Dr. Iltz states that the committee cannot say the others are not effective or they are not safe but in general that is exactly what the committee is saying by excluding them, so they need to back up and say which ones are safe and which are efficacious and then make a statement that says these are the ones we recommend for inclusion on the PDL and then let the department heads decide if that's what they go with or if they decide to go with something else, For example if department heads say we want all the generically available SSRI's and then we will also put buproprion on as well.
- Duane Thurman explains that as a non-clinician it sounds as if the committee wants to have all the drugs available on the PDL except for the one with the safety problem.
- *Many committee members speaking all at once, speech is unintelligible.*
- Dr. Lessler states that the committee is starting with the statement that the drugs are safe and effective. He commends Dr. Iltz for his suggestion and asks him now that the committee has listed all medications as safe and effective in the treatment of major depression, except nefazodone, which would be approached later, what the next step would be.
- Dr. Iltz suggests that the committee put together a recommendation to the department heads stating that specific set of drugs are those which should be included on the PDL, they do not have to be the ones that are safe and efficacious
- Dr. Lessler comments that there are certain drugs that the committee has agreed upon as being safe and effective, for example the committee has already decided that fluoxetine, mirtazapine, and buproprion must be available, and then rather than specifying two other SSRI's it would be best to instruct that fluoxetine plus two other SSRI's as that would provide some diversity.
- Dr. Reese comments that by doing so the committee would be returning to a more limited number of drugs and he adds that he agrees with Dr. Goo who suggested if the committee decided to recommend a narrow array of drugs it would be best to provide citalopram because of drug interactions. He suggests that both citalopram and fluoxetine be on the recommendation as well as mirtazapine and buproprion, with venlafaxine as a second line drug.
- Dr. Lessler comments that the committee seems to be coming closer to making a motion, he asks if anyone disagrees with those drugs which Dr. Reese mentioned, he also asks for suggestions in regards to additional first start medications
- Dr. Ballasiotes recommends that sertraline be available as he knows from experience that all these drugs work differently.
- Dr. Lessler reminds him that the committee is speaking of first starts.
- Dr. Ballasiotes recognizes this and goes on to say that the chemistry of each of the drugs in discussion different, that they are not like tricyclics.
- Patti Varley reiterates her concern with deciding which drugs are safe and efficacious and does not feel that the committee should leave drugs off the list.

- Dr. Lessler responds that committee has stated that all the drugs are safe and efficacious and now the committee is specifying which drugs should be on the list.
- Patti Varley asks on what basis the committee is selecting these drugs.
- Dr. Lessler replies that the committee is selecting each drug for specific reasons, citalopram has been selected because of its evidence for children and is an SSRI with the last drug-drug interaction, buproprion has been selected for its side effect profile.
- Dr. Marshall reminds the committee that during the review of the Proton Pump Inhibitor class they made the recommendation a drug be made available that is indicated in pediatrics that was shown to have fewer drug interactions, there are three drug classes here lumped into one. SSRI's, SNRI's and the others, the committee also specified that like with dihydropyridines and non-dihydropyridine it would be necessary to have one of each or more than one of each. So, a statement can be made to the effect that there needs to be pediatric indication and at least one drug with fewer drug interactions and potentially one from each of these different mechanisms of action.
- Dr. Bray comments that he feels that is what the committee was doing and that he is concerned that they have been delegating clinical decisions and that he is not sure that that is what the committee should do. He prefers the approach of identifying those drugs that have a unique nature and then adding plus and have an arbitrary number, one other two other from the SSRI category and then let the agencies choose.
- Dr. Lessler suggests the committee talk about the SSRI's for a moment, fluoxetine can be named along with another SSRI that has hew drug-drug interactions. HE asks of anyone on the committee suggests there be an additional SSRI
- Patti Varley provides an example in which a pediatric practitioner who understands what medications are approved and in clinical practice is faced with a child whose grandmother was on has been on six different antidepressants and failed several of them and only one had worked. The practitioner might then contact the grandmother to see which drugs failed for her and which one worked and try that as a first start as that might work the best with the family genome. Continuing the scenario, the practitioner has chose Zoloft, or some other non-preferred drug but neglects to write DAW.
- Dr. Lessler comments that this is a good point which pushes the committee forward to the decision regarding making a statement around therapeutic interchange
- Dr. Cordy feels the second sentence addresses that and she comment that it should read efficacious not effective in the first sentence.
- Dr. Marshall comments that the second sentence may be the source of the frustration. While the committee has said they are all safe and efficacious the second sentence and that there are no second generation antidepressants listed above is associated with fewer adverse events in special populations and this is where she suggests the committee is running into problems, because theses drugs do have different side effect profiles.
- Dr. Lessler suggested that the sentence be changed to say " above listed drugs shall not be subject to therapeutic interchange in the Washington State PDL for the treatment of major depression" take out that middle sentence about…
- Dr. Marshall suggests they say *(sound of coughing)*
- Dr. Bray feels that by saying that the drugs should not be subject to interchange that coves the issue about the fact that they do have side effects in different populations so its kind of a duplication in a sense, if that was taken out we get to the same place then we can decide which drugs based on the decisions we talked about should be on it and go from there
- Dr. Reese says I think before we have always named drugs we wanted on it, but we haven't just named well if you pick a drug from drugs that have fewer side effects if we want or pick a drug that is an atypical that we want, we've said drugs that we wanted for reasons that are clear to us, and I think we need to do that again we nee to keep that policy of naming the drugs that we think in each group are the ones we want on and others if needed
- Dr. Lessler comments that the next sentence be for example something to the effect of the PDL must include fluoxetine citalopram mirtazapine and buproprion.
- Dr. Reese suggests adding "and other as needed".
- *Many people talking all at once, discussion is unintelligible.*
- Dr. Bray suggests that the committee also add an arbitrary number of additional SSRI's so that we do- because if we did that what they could do in making the decision is isolate the list just to that group so if we really want more choice than we could arbitrarily say and two others from the SSRI category.
- Dr. Goo comments that if this is done we need to then state how many failures do you have before you move on to the other list, if you keep it like this then once you fail one of these drugs you can move on to wherever you want or if you want to increase the list of drugs on the PDL then I think you have to increase the number of times you fail one of these drugs on the list to move on. There are two ways you can approach that.
- Patti Varley expresses concern in regards to adding the middle sentence, from where I am sitting we have all said that they cannot be interchanged and that they all have unique reasons why a certain individual might need on or the other and if they are safe and efficacious.

- Dr. Bray if we don't say that something needs to be on it what we are, I mean we either say it includes all the list is that what you are arguing? I don't think that's necessary, and that we could pick some that must be on the list and leave the rest to the determination of the committee. But I also think instead of just leaving it like this where the only drugs could be those four I don't think that would be appropriate I think we need to have more, maybe we could add an arbitrary and let them choose.
- Dr. Lessler asks what would that number be.
- Dr. Reese suggests we don't have to state a number we can just leave it like these drugs have to be and other drugs can be added, that is how we have done it before, these drugs have to be on there it doesn't say others cant be added.
- Dr. Bray says but if we don't say that more should be added then what they could do is take that list and just include those four and I don't think that is appropriate.
- Dr. Marshall comments that is correct we could do that or you could say that we have to have these four in addition to x many others from the list that you feel will give you proper choice.
- Dr. Cordy says it seems like to the two big players here are sertraline and venlafaxine, those are the two that are not generic so I think we need to decide if we feel like on or the other or both of those ought to be included, if we don't think those two have to be included, then I don't think we have to put any additions on here, does anyone feel strongly that those two should be added to these four
- Janet Kelly comments just because they are generic does not mean the are going to be on the list so we need to specify if we want additional ones on there we cannot just leave it open.
- Dr. Cordy asks for the two that are not generic…even if they were generic do we feel like those should be included in addition to these four?
- Dr. Marshall says if you felt that they should have been on the list would you not have already included them in that four?
- Dr. Lessler asks Dr. Bray if they should say rather than try to specify two additional should we just expand the list of saying must include is that -what else would you want to see on there?
- Dr. Marshall replies that doctors can still write dispensed as written and get the non preferred drugs
- Dr. Iltz thinks that what we have is good and I am confident that the people who are going to look at this and make the ultimate PDL decision for these four and any additional ones can do that and so from my standpoint I think that without tying our hands any further and saying must do this and must do that we have already which ones we think are the most appropriate and I think we should just leave it at this a t this point.
- Dr. Bray surrenders
- Dr. Lessler responds that he is fine with this as well.
- Patti Varley feels she is still struggling with if we say they are all equally safe and efficacious and we discussed why we would pick certain ones under certain circumstances that were safe and efficacious how we then pick those four.
- Dr. Thompson feels that is within your purview if we were just to rely on OHSU reports which I think was the idea of 6088 it was to also have the clinical expertise here to make sure that negative evidence was not driving the decision so your clinical expertise in incredibly important in this and I feel that is in your purview what you are doing is telling the physician community this is what your recommendations are for at least a new start and then staff are taking direction that at least for refill and for other things working with the stakeholder group if there are some criteria we will work with you on that in the DUR portion.
- Dr. Lessler makes a comment sort of related to Patty's point if for example the PDL contained those four meds if then a provider wrote for venlafaxine and did not write DAW that could not be therapeutically interchanged there would have to be a conversation which might lead to venlafaxine be dispensed after there was clarification around why that was written.
- Dr. Thompson says that is correct given your last statement about no interchange.
- Dr. Marshall ask Patti Varley if it would it be easier for you to say in the second sentence I understand what you are saying we are saying these four must be on the list because there is something special about them if we put in there that there are subgroups associated with side effects or different efficacy that we would think that should be on the list.
- Dr. Lessler comments that he is not sure he understands what Dr. Marshall is saying
- Dr. Marshall comments that we are not saying they are equally safe and effective we are saying that they are safe and efficacious the difference is though that there are subpopulation or are different side effect profiles of these drugs so you feel that there needs to be at least these four……..
- Dr. Lessler states that he feels that is implicit in the motion
- Dr. Marshall comments that she was attempting to clarify the situation.

Dr. Reese: After considering the evidence of safety, efficacy and special populations for the treatment of MAJOR DEPRESSIVE DISORDER, I move that CITALOPRAM, ESCITALOPRAM, FLUOXETINE, SERTRALINE, FLUVOXAMINE,

PAROXETINE, MIRTAZAPINE, VENLAFAXINE, BUPROPRION are safe and efficacious. The Preferred Drug List must include fluoxetine, citalopram, mirtazapine, and buproprion. THE SECOND GENERATION ANTIDEPRESSANTS shall not be subject to therapeutic interchange in the Washington preferred drug list for the treatment of MAJOR DEPRESSIVE DISORDER. …. (Read off of the projected screen)
2nd: *was seconded but the speaker did not identify him/herself*

- Dr. Lessler invites further discussion.
- Dr. Ballasiotes repeats his request to add sertraline to the list.
- Dr. Lessler suggests a vote.

Vote: Motion carries.

Non-Sedating Antihistamines

Susan Carson gives presentation via conference phone.

The tape for this meeting failed to record the last thirty minutes of the session. The text below is gathered from notes taken during the meeting.

Stakeholder Input

Dr. Lessler asks that the stakeholders keep comments to three minutes or less and that they identify any sponsors and submit all evidence to OHSU

- Penny Nelson of the Asthma and Allergy Foundation reminds the committee that while there is no scientific evidence of difference, from experience with the 1-800 line she understand that each individual is different and one drug does not address all individuals needs.
- Jonathan Raap, a representative of Medical Affairs with Sanofi Aventis, found that when reviewing antihistamines, clinical efficacy and safety patient variability in terms of response all of these drugs there was no difference statistically between agents, but that fexofenadine has demonstrated good effects.
- Gokul Gupalan, M.D., of Schering-Plough, speaks to the use of clarinex, detailing its benefits in terms of slow metabolizers in black
- David Shoen, M.D., a primary care practitioner who deals mostly with pediatric patients, urges the committee to consider cetirizine in all dosing modalities available and allow that both syrup and chewable tablets and pills be made available.
- Dr. Chan, a practicing oterlaryngologist?, speaks to the treatment of allergic and non- allergic rhinitis, he feels that it is very limiting just using one drug, he feels that Zyrtec in chewable form is a good choice for children down to the age of six months. He feels that the current system of prior authorization is very time consuming and he feels is Zyrtec in chewable form were made available for children and aged population it would help him to treat his patients more effectively.
- Dave Gross, a clinical pharmacist with Pfizer Pharmaceuticals, comments that satirizine and zyrtec have shown safety and efficacy and both are available in syrup and chewable form for children and those individuals who cannot take tablets.

Committee Deliberation and Vote

- Dr. Lessler suggests that the committee deliberate again before attempting to craft a motion.
- Dr. Bray asks Susan (last name?) if there is further information regarding the reactions that the 2nd generations have versus first generation
- Susan responds that the adverse reactions were about sedations and performance impairment.
- Dr. Lessler asks the committee if there are any further questions or suggestion before a motion is made
- Dr. Bray comments that he has a couple thoughts regarding the fairly small group of drugs in this particular class, one of the concerns would be side effects and special populations, specifically in pregnant patients and he feels that considering the risk the committee should have a "b" rated drug. He also feels that satirizine is more sedating than the others and this is the differentiation he sees among the drugs.
- Dr. Reese agrees that all are equally efficacious except for satirizine being more sedating.
- Dr. Bray reminds the committee that it is important to have some pediatric formulation.
- Dr. Reese comments that liquid and chewable tablet be made available.

- Dr. Goo comments that allergic rhinitis would be second level/
- Dr. Lessler feels the committee is working toward creating a motion in which they would state that these drugs are equally efficacious and safe listing which drugs should be on the formulary, one that is less sedating, one that is category b and one that is in liquid form.
- Dr. Iltz comments that there is an over the counter preparation, he wonders if the committee should treat this class as they did ARB's with the understanding that they are available.
- Dr. Reese comments that Medicaid patients can get over the counter medication with a prescription.
- Dr. Childs mentions that MAA has over the counter medications listed as preferred.
- Lessler my sense is that that meets our requirements that we have laid out in terms of basic frame work, can we just frame this as with no change to current PDL.

> **Dr. Cordy:** After considering the evidence of safety, efficacy and special populations for the treatment of SEASONAL ALLERGIC RHINITIS, PERENNIAL ALLERGIC RHINITIS, AND CHRONIC IDIOPATHIC URTICARIA, I move that CETIRIZINE, DESLORATADINE, LORATADINE, AND FEXOFENADINE are safe and efficacious. The Washington Preferred Drug List should contain loratadine. NON-SEDATING ANTIHISTAMINES can be subject to therapeutic interchange in the Washington preferred drug list for the treatment of SEASONAL ALLERGIC RHINITIS, PERENNIAL ALLERGIC RHINITIS, AND CHRONIC IDIOPATHIC URTICARIA.
> **2nd:** Dr. Reese
> **Vote:** Motion carries

2:25 meeting adjourned.

DUR Board Meeting Minutes
February 16, 2005

WASHINGTON STATE PHARMACY AND THERAPEUTICS COMMITTEE MEETING
Regular Meeting
Radisson Hotel SeaTac

2:00pm – 4:00pm

Council Members Attending: Alvin Goo, Pharm D, Patti Varley, ARNP, Carol Cordy, MD, Dan Lessler, MD, Robert Bray, MD, T. Vyn Reese, Angelo Ballasiotes, Pharm D., Jason Iltz, Pharm D., and Janet Kelly, Pharm D. John White, PA, was present by conference call.

Medical Assistance Administration, Coordinating Staff: Jeff Thompson, MD, MAA Chief Medical Officer; Siri Childs, Pharm D, Pharmacy Policy Manager; MAA, and Nicole Nguyen, Pharm D, Clinical Staff Pharmacist, MAA

I. ADMINISTRATIVE ITEMS

The meeting was brought to order by Chairman, Dan Lessler, MD. The minutes of the previous DUR Board Meeting in December, 2004 were approved.

II. "A CLINICALLY SOUND APPPROACH TO MEDICAID COST CONTAINMENT – PSYCHOTHERAPEUTICS"

Mental Health Drug Work Group Business Plan Update

Jeff Thompson, MD provided the attached presentation to report on the last two mental health stakeholder meetings.

The next steps for addressing duplicate second generation antidepressant therapy will be communication with and education of prescribers. MAA will do academic detailing face to face or in writing in addition to a questionnaire. The questionnaire will provide MAA and stakeholders with information of whether the prescribers were aware of the duplicate therapy and what the reasons are for the duplicate therapy. The results will assist in developing criteria for a hard stop in the future. In a past intervention MAA sent out letters to prescribers of patients with duplicate therapy in 2002. There was a 53% response rate, and of the responses 19% were a discontinuation of an order.

Dr Bray believed the questionnaire was a good idea but cautioned that some of the questions imply that there are right answers and they were not just to gather information for MAA. MAA should consider providing information on the best practice as well as asking the questions or just ask questions in a way to does not imply there are correct answers.

The DUR board discussed patients seeing multiple providers, and medications being changed without discontinuation of the first antidepressant as two situations that could lead to unintentional duplication of antidepressant therapy.

Patty Varley expressed concern about therapy being denied for outliers when good rationale is provided for the duplicate antidepressant therapy. MAA will accept good rationale for duplicate therapy provided by the prescriber for approving duplicate therapy.

At this time MAA is gathering information from the communication with providers to learn exceptions for when duplicate therapy is needed. Mechanism of action may be considered for the second generation antidepressants. At this time hard stops would only be implemented for the SSRIs. Duplicate second generation antidepressants intervention is only educational at this time. Duplication will be defined as more than a 60 day overlap in a 90 day period to account for patients being tapered off of one antidepressant and started on another antidepressant. Providers will be getting a 2 month warning with the educational intervention before a hard stop is started.

III. MANUFACTURERS' PRESENTATION

There were no stakeholder's presentations to the DUR Board

IV. STAKEHOLDERS' PRESENTATIONS

There were no stakeholder's presentations to the DUR Board

V. RECOMMENDATIONS OF COUNCIL

- The DUR Board all voted in favor of endorsing the Mental Health Stakeholder Work Group in regard to the targeted prescription initiative.

- Dr Bray suggested that patients who the intervention is done on should be followed to see if other health care expenditures increase, decrease or stay the same after the intervention.

VI. ANNUAL DUR REPORT ASSIGNMENTS

Dr Childs handed out the DUR Annual Report assignments. Last year's report and meeting minutes for the last Federal fiscal year will be sent out by email and hard copy to members.

ADJOURNMENT